

WHAT IS CLAIMED IS:

1. A method for the selective enhancement of the expression of a protein in a tumor cell characterized by aberrant Wnt signaling comprising treating said tumor cell with an effective amount of a
5 retinoid.
2. The method of claim 1 wherein said protein is characterized by synergistic enhancement of its expression by a combination of Wnt-1 and said retinoid.
3. The method of claim 2 wherein said protein is a cell surface protein.
4. The method of claim 2 wherein said protein is over-expressed in tumor cells relative to
10 corresponding normal cells.
5. The method of claim 2 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1, ISLR, autotaxin, and Stra6.
6. The method of claim 5 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1, ISLR, and Stra 6.
7. The method of claim 6 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1, and ISLR.
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8. The method of claim 1 wherein said retinoid is a retinoic acid.
9. The method of claim 1 wherein said tumor is a human cancer.
10. The method of claim 9 wherein said human cancer is selected from the group
20 consisting of ovarian cancer, endometrial cancer, Wilm's kidney tumor, colon cancer, breast cancer, prostate cancer, gastric cancer, lung cancer, hepatocellular cancer, and melanoma.
11. A method for the treatment of a tumor characterized by aberrant Wnt signaling comprising treating said tumor with an effective amount of a combination of a retinoid and an anti-tumor agent, wherein said anti-tumor agent targets a protein in said tumor the expression of which is enhanced
25 by retinoid treatment.
12. The method of claim 11 wherein the expression of said protein is synergistically enhanced by a combination of Wnt-1 and a retinoid.
13. The method of claim 11 wherein said protein is a cell surface protein.
14. The method of claim 11 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1, ISLR , autotaxin and Stra6.
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15. The method of claim 14 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1, ISLR and Stra 6.
16. The method of claim 15 wherein said protein is selected from the group consisting of 4-1BB ligand, ephrin b1 and ISLR.
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17. The method of claim 11 wherein said retinoid is administered prior to the administration of said anti-tumor agent.

18. The method of claim 11 wherein said retinoid is administered concurrently with the administration of said anti-tumor agent.

19. The method of claim 11 wherein said retinoid is administered following the administration of said anti-tumor agent.

5 20. The method of claim 11 wherein said anti-tumor agent is an antibody.

21. The method of claim 20 wherein said antibody is an antibody fragment.

22. The method of claim 21 wherein said antibody fragment is selected from the group consisting of Fab, Fab', F(ab')₂, and Fv fragments, diabodies, single-chain antibody molecules, and multispecific antibodies formed from antibody fragments.

10 23. The method of claim 20 wherein said antibody is a chimeric antibody.

24. The method of claim 20 wherein said antibody is a humanized antibody.

25. The method of claim 20 wherein said antibody is a human antibody.

26. The method of claim 20 wherein said antibody is conjugated to a cytotoxic agent.

27. The method of claim 26 wherein said cytotoxic agent is a toxin.

15 28. The method of claim 27 wherein said toxin is a maytansinoid.

29. The method of claim 20 wherein said antibody is produced in CHO cells.

30. The method of claim 20 wherein said antibody is produced in bacteria.

31. The method of claim 20, further comprising treatment with a chemotherapeutic agent.

32. The method of claim 20, further comprising radiation treatment.

20 33. The method of claim 11 wherein said tumor is a human cancer.

34. The method of claim 33 wherein said human cancer is selected from the group consisting of ovarian cancer, endometrial cancer, Wilm's kidney tumor, colon cancer, breast cancer, prostate cancer, gastric cancer, lung cancer, hepatocellular cancer, and melanoma.

35. A method for identifying a gene target for tumor treatment comprising:

25 (a) contacting a cell expressing a Wnt proto-oncogene with a retinoid;

(b) determining the gene expression profile of said cell; and

(c) identifying a gene the expression of which is enhanced by said retinoid treatment relative to its expression in a corresponding untreated cell, as a target for tumor treatment.

36. The method of claim 35 wherein said cell is engineered to conditionally express said

30 Wnt proto-oncogen.

37. The method of claim 36 wherein said proto-oncogen is Wnt-1.

38. The method of claim 36 further comprising the step of inducing the expression of said Wnt-1 and identifying a gene the expression of which is synergistically enhanced by said tumor treatment and Wnt-1 signaling, as a target for tumor treatment.

35 39. The method of claim 35 wherein said cell is a tumor cell.

40. The method of claim 35 comprising identifying a gene the expression of which is selectively enhanced by said retinoid treatment relative to a normal cell treated with said retinoid, as a target for tumor treatment.

41. The method of claim 39 wherein said tumor cell is from a frozen tumor sample.

5 42. The method of claim 41 wherein said tumor cell is from a paraffin-embedded, formalin-fixed tumor sample.

43. The method of claim 35 wherein the gene expression profile is determined by reverse transcriptase-PCR (RT-PCR) analysis.

10 44. The method of claim 35 wherein the gene expression profile is determined by *in situ* hybridization.

45. The method of claim 35 wherein the gene expression profile is determined by northern blotting.

15 46. A method for the treatment of a tumor in a mammalian subject comprising the steps of:
(a) incubating a sample of said tumor with a retinoid;
(b) determining the gene expression profile of said sample prior to and following said incubation;
(c) identifying a gene the expression of which is enhanced by said retinoid; and
(d) treating said patient with a combination of a retinoid and an anti-tumor agent targeting said gene.

20 47. The method of claim 46 wherein said sample is additionally incubated with Wnt-1.

48. The method of claim 47 comprising identifying, in step (c) a gene the expression of which is synergistically enhanced by a combination of said retinoid and Wnt-1.

25 49. The method of claim 46 wherein said anti-tumor agent is an antibody.

50. The method of claim 49 wherein said antibody is an antibody fragment.

51. The method of claim 50 wherein said antibody fragment is selected from the group consisting of Fab, Fab', F(ab')₂, and Fv fragments, diabodies, single-chain antibody molecules, and multispecific antibodies formed from antibody fragments.

30 52. The method of claim 49 wherein said antibody is a chimeric antibody.

53. The method of claim 49 wherein said antibody is a humanized antibody.

54. The method of claim 49 wherein said antibody is a human antibody.

55. The method of claim 49 wherein said antibody is conjugated to a cytotoxic agent.

56. The method of claim 55 wherein said cytotoxic agent is a toxin.

57. The method of claim 56 wherein said toxin is a maytansinoid.

58. The method of claim 49 wherein said antibody is produced in CHO cells.

35 59. The method of claim 50 wherein said antibody is produced in bacteria.

60. The method of claim 46 further comprising treatment with a chemotherapeutic agent.

61. The method of claim 46 further comprising radiation treatment.

62. A method for diagnosing a cancer characterized by aberrant Wnt signaling in a mammalian subject comprising

- (a) contacting a biological sample obtained from said patient with retinoic acid;
- (b) detecting the gene expression profile in said biological sample; and

5 (c) detecting a tumor antigen the expression of which is enhanced by said retinoid treatment.

63. The method of claim 62 wherein said tumor antigen is selected from the group consisting of 4-1BB ligand, ephrin b1, ESLR, autotaxin, and Stra6.

64. An article of manufacture comprising:

10 a container;
an anti-tumor agent within said container; and
instructions to administer said anti-tumor agent in combination with a retinoid.

65. The article of manufacture of claim 64 further comprising a retinoid.

66. The article of manufacture of claim 65 wherein said retinoid is a retinoic acid.

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